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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/073,464	02/11/2002	James Tiedje	MSU-06787	4392

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EXAMINER	
BAUSCH, SARAE L	
ART UNIT	**PAPER NUMBER**
1634	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/073,464	TIEDJE ET AL.	
	Examiner	Art Unit	
	Sarae Bausch	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 October 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-6,8-14 and 22-27* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6,8-14 and 22-27* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 10/24/2007 has been entered.

2. Currently, claims 1-6, 8-14, 22-27 are pending in the instant application. Claim 7 and 15-21 have been canceled and claims 22-27 have been added. This action is written in response to applicant's correspondence submitted 10/24/2007. All the amendments and arguments have been thoroughly reviewed but were found insufficient to place the instantly examined claims in condition for allowance. The following rejections are either newly presented or are reiterated from the previous office action. Any rejections not reiterated in this action have been withdrawn as necessitated by applicant's amendments to the claims. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action. **This action is Non-Final.**

Withdrawn Rejection

3. The rejections of claims 1-6 and 8-14, under 35 U.S.C. 102 (e), made in section 4 of the previous office action mailed 06/18/2007, is withdrawn in view of the amendment to the claims.

4. The rejections of claims 1-6 and 8-14, under 35 U.S.C. 102 (e), made in section 6 of the previous office action mailed 06/18/2007, is withdrawn in view of the amendment to the claims.

5. The rejection of claims 1-5 and 8-13 under 35 USC 103(a) made in section 9 of the office action mailed 06/18/2007 is withdrawn in view of the amendment to the claims.

6. The rejection of claims 6 and 14 under 35 USC 103(a) made in section 11 of the office action mailed 06/18/2007 is withdrawn in view of the amendment to the claims.

Claim Rejections - 35 USC § 112

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 22-25 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Newly added claims 22-25 with the recitation of "at least 60 arrayed elements" and "at least 90 arrayed elements" and the subgenus of "at least 60" and "at least 90" is not supported in the specification and raises the issue of new matter. The specification teaches 60 to 96 genome fragments were spotted on microarrays (see page 7, lines 5-6). The specification teaches that arrays containing up to approximately 100,000 DNA spots are used (see page 7, lines 20-22). However the specification does not teach "at least" 60 or "at least" 90 arrayed elements. The specification provides no indication of the criticality of the amended range.

As discussed in MPEP 2163.05, section III, with respect to changing numerical range limitations, the analysis must take into account which ranges one skilled in the art would consider inherently supported by the discussion in the original disclosure. Purdue Pharma L.P. v. Faulding Inc., 230 F.3d 1320, 1328, 56 USPQ2d1481, 1487 (Fed. Cir. 2000) ("[T]he specification does not clearly disclose to the skilled artisan that the inventors... considered the... ratio to be part of their invention.... There is therefore no force to Purdue's argument that the written description requirement was satisfied because the disclosure revealed a broad invention from which the [later-filed] claims carved out a patentable portion").

Claim Rejections - 35 USC § 103

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

10. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

11. Claims 1-6, 8-14, and 22-27 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gingeras et al. (US Patent 6228575) in view of Hayward et al. (Mol. Microbiology, 2000, 35(1), 6-14) as evidenced by DiResi (cited on 892 filed 11/19/2003).

With regard to claim 1 and 9, Gingeras et al. teach a method of oligonucleotide array for speculating and phenotyping organism by providing an array of known locations on a substrate comprising a plurality probes to reference DNA sequences hybridizing target nucleic acid sequence to array and based on hybridization pattern identifying the genotype of the first organisms(see column 3, lines 1-13 and column 4, lines 7-13). Gingeras et al. teach amplification of nucleic acid sample prior to hybridization (See column 8, lines 34-37) (providing amplified genomic sequences). Gingeras et al. teach hybridized nucleic acid are detected by detecting one or more labels attached to the sample nucleic acids and include fluorescein labels (see column 8, lines 46-57) (labeled DNA with a fluorescent dye). Gingeras et al. teach the screening method allows one to build up a data base of hybridization patterns corresponding to different species. Gingeras et al. teach identifying mycobacterium species by measuring fingerprint data (hybridization pattern on array) (see column 30, lines 65-67) by a collection of samples and based on these measurements a systematic way to predict species of each member of the collect by comparing the signal produced by the target at each hybridization site compared to the signal produced by Mt rpoB (see column 31, lines 1-5). Specifically, Gingeras et al. teach hybridization analysis of 7 mycobacteria species (reference samples) and teach that a reference sequence can be sequence of nucleotides, DNA (see column 12, lines 51-53 and column 34, lines 45-51). Gingeras et al. teach fluorescently labeled amplicons from mycobacteria species hybridized to a DNA chip and comparing the hybridization pattern to

amplicons hybridized to the DNA chip from M. tuberculosis (test bacteria) (see column 35, lines 15-25 and table 4). Gingeras et al. teach analyzing the fingerprint pattern of each species followed by classification analysis (calculating the hybridized DNA fluorescent dye signal and reference DNA fluorescence to determine identity) (See column 36, lines 35-51).

With regard to claim 2-3 and 10-11, Gingeras et al. teach assaying biological samples, which refers to a sample obtained from an organism or clinical sample from a patient (See column 8, lines 22-34).

With regard to claim 4 and 12, Gingeras et al. teach assaying biological samples obtained from an organism (environmental sample) (see column 8, lines 22-25).

With regard to claim 6, 13, 14, and 26-27, Gingeras et al. teach hybridization patterns (producing hybridization profiles) correlated to species determination using mathematical pattern recognition algorithms (calculating by statistical analysis) (see column 30, lines 5-67 and column 31, lines 1-67).

With regard to claims 22-25, Gingeras teach array with a lower limit of 25, 50, or 100 probes to as many as 10^4, etc. probes (See column 16, lines 1-6)

Gingeras does not teach random amplified genomic sequences that are 1-2kb arrayed on a solid support.

Hayward et al. teach constructing a shotgun DNA microarray using random inserts from a genomic library and allows for analysis of genomes that have not been fully sequenced (see abstract). Hayward teach constructing a DNA microarray by printing 3648 PCR amplified inserts from a DNA library. Hayward et al. teach amplified inserts from 8000 independent clones were applied to the array and the average size was 1-2 kb (see pg. 7, array construction).

Hayward teach labeling two different forms of Plasmodium with two different fluorescent labels to evaluate the differences among the two forms (see pg. 7, 2nd column, last paragraph). Hayward teach that fluorescence signals from Cy3 and Cy5 label were separately measured at each spot on the array and the red/green fluorescence ratio provided a measure of the relative abundance of the transcripts (see pg. 8, 1st column, 1st para). It is noted that Hayward teaches hybridized cDNA on glass arrays were processed and analyzed for fluorescence as previously described by DeRisi. DeRisi et al. reference discloses that processing and recording of signals comprises calculation of a hybridization signal intensity ratio and normalization of the signal (claims 6, 14, 26 and 27) (see footnote 49 of DeRisi), accordingly it is an inherent property of the method of Hayward to include such a step.

Therefore, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to improve the method of determining the species of an organism by providing a substrate comprising a plurality probes to reference DNA sequences as taught by Gingeras to include a shotgun DNA microarray of reference DNA sequences from multiple organisms as taught by Hayward to allow for a more robust analysis of phenotyping organisms to include detection of unsequenced genomes. The ordinary artisan would have been motivated to include the method of constructing a shotgun DNA microarray as taught by Hayward in the method of Gingeras because Gingeras teach that other sequences can be detected in the method (see column 9 lines 20-25) and Hayward to teach that the microarray allows for analysis of genomes that have not yet been sequenced. Furthermore, because both Gingeras and Hayward to analysis of genomic sequences of pathogenic organisms by DNA hybridization of microarrays, it would have been obvious to one of ordinary skill in the art to substitute one method, the

construction of the shotgun microarray as taught by Hayward for the array of probes specific for rpoB gene as taught by Gingeras in order to achieve the predictable result of detecting bacterial species using DNA hybridization patters using a DNA microarray.

Response to Arguments

12. The response asserts that Gingeras cannot be practiced using random sequences and that Gingeras teach that the sequence of a selected gene must be known. This response has been thoroughly reviewed but not found persuasive. Although Gingeras teach using known sequences of the rpoB gene, Gingeras teach that any gene sequence can be used (see column 9, lines 20-25). Furthermore, Gingeras teach that a tiling strategy using multiple probe sets (see column 10, lines 14-16) and teach arrays of all possible probes of a given length can be used (see column 16, lines 8-18). A tiling strategy of a microarray or an array of all possible probes of a given length will include random sequences and therefore the method of Gingeras could be practiced using random amplified sequences from different organisms.

13. Claims 1-5, 8-13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Greisen et al. (J.Clin. Microbial. 1994, vol. 32, pp 335-351) in view of Hayward as evidence by DeRisi (Science, 1997, 278:680-686, cited on 892 filed 11/19/2003).

Greisen et al. teaches a method of detecting DNA for the identification of over 60 different strains representing 18 different bacterial species found as pathogens (instant claim 3 and 11) or presumptive contaminants in human CSF (see page 336, 1st column, 1st paragraph). Greisen et al. exemplifies amplifying DNA using universal primers, followed by gel

electrophoresis of amplified products, and blotting the gel onto a Pall Biodyne membrane and fixing the DNA to the membrane by a UV crosslinker (random amplified genomic DNA arrayed on a solid support, microchip) (instant claim 5) (see page 336, 1st column, last paragraph cont'd to 2nd column). Greisen et al. teach probes of target DNA and reference DNA labeled with ^{32}P (see probe hybridization, page 338 and table 3) and hybridization of target DNA probes and reference DNA probes hybridized to DNA blots in 5xSSPE. Greisen et al. teach up to 12 meningitis and contaminant probes (reference and test DNA) tested against seven major bacterial species causing meningitis and identification of bacteria in CSF based on the hybridization pattern of each probe (instant claim 8 and 13) (see page 346, 2nd column, last two paragraph and table 4). Greisen et al. teaches that the use of the panel of probes would enable a single CSF sample to obtain multiple probe hybridization results and form a more rapid and sensitive means of detecting bacteria in clinical samples (see page 350, 1st column, last paragraph). Greisen et al. does not teach the use of fluorescence detection for hybridization.

Hayward et al. teach constructing a shotgun DNA microarray using random inserts from a genomic library and allows for analysis of genomes that have not been fully sequenced (see abstract). Hayward teach constructing a DNA microarray by printing 3648 PCR amplified inserts from a DNA library. Hayward et al. teach amplified inserts from 8000 independent clones were applied to the array and the average size was 1-2 kb (see pg. 7, array construction). Hayward teach labeling two different forms of Plasmodium with two different fluorescent labels to evaluate the differences among the two pathogenic forms (see pg. 7, 2nd column, last paragraph). Hayward teach that fluorescence signals from Cy3 and Cy5 label were separately measured at each spot on the array and the red/green fluorescence ratio provided a measure of

the relative abundance of the transcripts (see pg. 8, 1st column, 1st para). Hayward teaches hybridized cDNA on glass arrays were processed and analyzed for fluorescence as previously described by DeRisi. DeRisi et al. reference discloses that processing and recording of signals comprises calculation of a hybridization signal intensity ratio and normalization of the signal (claims 6, 14, 26 and 27) (see footnote 49 as DeRisi) accordingly it is an inherent property of the method of Hayward to include such a step.

Therefore, it would have been prima facie obvious to improve the method of detection of bacteria in a sample using southern blot hybridization as taught by Greisen et al. to include a shotgun DNA microarray to allow for high-throughput analysis using fluorescence detection hybridization as taught by Hayward et al. The ordinary artisan would have been motivated to improve the method of the southern blot hybridization method as taught by Greisen et al. to include a more rapid, automated method of multiplexing for the identification of pathogens in bacteria as taught by Hayward et al. because Hayward et al. suggests using different labeled probes for combining different nucleic acid sample and also the use of the shotgun DNA microarray for analysis of genomes that have not yet been sequenced for the possibility of multiplexing. Furthermore, the ordinary artisan would be motivated to use fluorescent-labeled probes to eliminate the use of radioactivity, as fluorescence in non-radioactive. The ordinary artisan would have had a reasonable expectation of success that the use of fluorescent-labeled probes to detect pathogens could be used in the method of Greisen et al. because Hayward et al. teach the use of fluorescent-labeled probes hybridizing to a sample for the detection of pathogens. The ordinary artisan would have had a reasonable expectation of success that the use of shotgun DNA microarray could be used in the method of Greisen et al. because Greisen et al.

teaches the use of panel of probes that would enable the use of a single CSF sample to obtain multiple probe hybridization results and form a more rapid and sensitive means of detecting bacteria in clinical samples.

Conclusion

14. No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sarae Bausch whose telephone number is (571) 272-2912. The examiner can normally be reached on M-F 9am-5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached on (571) 272-0735. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at (866) 217-9197 (toll-free).

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

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Sarae Bausch, PhD
Examiner
Art Unit 1634